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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/880,457	06/12/2001	James Pan	P2871R1	5233

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EXAMINER
DEBERRY, REGINA M

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 12/16/2002

12

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/880,457	PAN ET AL.	
	Examiner	Art Unit	
	Regina M. DeBerry	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 October 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-48* is/are pending in the application.

4a) Of the above claim(s) *19-48* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-48* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *01 October 2001* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *7* .
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other: .

Status of Application, Amendments and/or Claims

The information disclosure statement filed 07 March 2002 (Paper No. 7) was received and complies with the provisions of 37 CFR §§1.97 and 1.98. It has been placed in the application file and the information referred to therein has been considered as to the merits.

Applicant's election of Group I (claims 1-18. SEQ ID NO:1, SEQ ID NO:4 and ATCC Deposit PTA-3376) in Paper No.11 (11 October 2002) is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). However, Applicant states, "As this portion of the Examiner's request is really an election of species, and not a restriction, the Examiner is reminded of M.P.E.P 809.02(c) (B) (I)...."

Contrary to Applicant's assertion, this is not the case. Each sequence (SEQ ID NO:) is patentably distinct because they are composed of unrelated or diverse sequences, different coding regions and/or imparts structural and functional differences. The request for an election of a single polynucleotide, polypeptide and ATCC Deposit No. was not a species election but a further election of a group.

Claims 19-48 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected Group, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 11.

Priority

Based on the information disclosed by Applicant and an inspection of the instant application, the Examiner has concluded that the subject matter defined in this application, specifically SEQ ID NO:1, SEQ ID NO:4 and ATCC Deposit No. PTA-3376 (DNA 146649-1789R1) is not supported by the disclosure in Provisional Application No. 60/212,901 filed 20 June 2000. Accordingly, the subject matter defined in claims 1-18 have an effective filing date of 12 June 2001. Should the Applicant disagree with the Examiner's factual determination above, it is incumbent upon the Applicant to provide specific page and line numbers of the provisional application which specifically supports the particular claim limitation for each and every claim limitation in all the pending claims which Applicant considers to have been in possession of and fully enabled for prior to 12 June 2001.

Drawings

The drawings are objected to as failing to comply with 37 CFR 1.84(p)(5) because they include the following reference sign(s) not mentioned in the description: Figures 3A-3C. Example 11 (specification, page 103) is drawn to experiments employed in transgenic mice, but fails to refer to the transgenic mice figures (Figures 3A-3C or any other appropriate figures), which are part of the investigation. The specification should be checked to ensure that all of the figures are referred to. No new matter may be added.

A proposed drawing correction, corrected drawings, or amendment to the specification to add the reference sign(s) in the description, are required in reply to the

Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance.

Claim Objections

Claims 1-9,11 and 15 and objected to because of the following informalities:

Claims 1-9, 11 and 15 encompass non-elected inventions (SEQ ID NO: and ATCC Deposit No.) and require amendment to limit to elected invention. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 6, 7, 8, 9,10, 11, 12 and 18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 6 and 7 are indefinite because the instant claims are drawn to an isolated nucleic acid molecule comprising DNA having at least 80% nucleic acid sequence identity to the full-length polypeptide **coding sequence** of the human cDNA deposited with the ATTC. A coding sequence is nucleic acid.

Claim 9 is indefinite because it is unclear what the claim is intended to encompass. It is suggested to delete "that" in the 1st line of claim 9 and change "comprising" to "comprises" in the 3rd line of claim 9.

Claims 8, 10 and 11 are indefinite because stringency is relative, and the art does not recognize a single set of conditions as stringent. The specification also does not provide an unambiguous definition for the term. In the absence of a recitation of clear hybridization conditions (e.g., "hybridizes at wash conditions of A X SSC and B % SDS at CoC"), the claims fail to define the metes and bounds of the varying structures of polynucleotides recited in the claimed methods.

Claim 12 is indefinite because it refers back to claim 12. The metes and bounds of the claim cannot be determined.

Claim 18 is indefinite because it ultimately depends from claim 1, which recites a complement of the DNA molecule. A polypeptide cannot be produced from the complement of an isolated nucleic acid molecule.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-18 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a credible, specific and substantial asserted utility or a well established utility.

The claims are directed to polypeptides NS4 and nucleic acids encoding the polypeptides. The specification states that the genes are involved in the control of mammalian body weight and compounds, which modulate the expression and/or activity of NS4 polynucleotide, can be useful as therapeutic agents in the treatment of mammalian body weight disorders.

The data disclosed is insufficient to support a utility because it is not clear how the DNA or encoded protein affects body weight or is involved in the control of body weight. Many of the relevant experimental parameters and details are missing. There is no indication in Example 11 which cDNA encoding NS4 was employed to make the transgenic mice. There is no reference to any figures that supports the data. It is unclear if the standard lab chow feed to the mice was high fat or low fat (page 103, lines 24-29). The specification fails to disclose the length of time the transgenic and control mice were fed the lab chow before measurements were recorded. It is unclear if the instant invention affects endpoint body mass or growth rate.

The instant application has failed to provide guidance as to how one of skill in the art could use the claimed invention in a way that constitutes a credible, specific or substantial utility. The proposed uses of the claimed invention are simply starting points for further research and investigation into potential practical uses of the claimed polypeptide.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-18 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a credible, specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Furthermore, claims 1-7, 11-14, 16-18 are drawn to an isolated nucleic acid molecule which comprises DNA having at least 80% sequence identity to a DNA encoding a NS4 polypeptide and an isolated nucleic acid molecule comprising at least 31 nucleotides. The specification is not enabled for variants and fragments.

The specification does not teach how to make any variant of NS4 polypeptides and provides no assay to evaluate the function of any modified polypeptide. Absent any means to assess the function of the polypeptide, it would require an indeterminate quantity of fundamentally unpredictable investigational experimentation of the skilled artisan to determine whether any modified polypeptide could be used in the same manner as the native exemplar. Such experimentation would be undue for one skilled in this art.

Furthermore, even were an assay provided, the specification would not support claims to polynucleotides encoding NS4 polypeptides modified to an unlimited extent relative to those exemplified. In order to make a sequence variant, for example, with the

reasonable assurance that it would have the desirable properties of the invention, the artisan would need to know which regions of the disclosed polypeptide are responsible for the interactions underlying its biological function(s). As is well recognized in the art, any modification (even a "conservative" substitution) to a critical structural region of a protein is likely to significantly alter its functional properties. It is known for nucleic acids as well as proteins, that even a single nucleotide or amino acid change or mutation can destroy the function of the biomolecule in many cases. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. These or other regions may also be critical determinants of antigenicity. These regions can tolerate only relatively conservative substitutions or no substitutions (see Wells, 1990, Biochemistry 29:8509-8517).

The disclosure provides no guidance as to which regions of the protein would be tolerant of modification and which would not, and it provides no working example of any variant sequence which would be within the claims. It is in no way predictable that randomly selected mutations, deletions, *etc.* in the disclosed sequence would afford a protein having activity comparable to the one disclosed. Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. Without sufficient guidance, the changes which can be made in the structure and still maintain sufficient activity is unpredictable and the experimentation left to those skilled in the art is unnecessarily and improperly extensive and undue.

Due to the large quantity of experimentation necessary to generate the infinite number of derivatives recited in the claims and possibly screen same for activity, the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide activity, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of the effects of mutation on protein structure and function, and the breadth of the claims which fail to recite any structural or functional limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Claims 1-7, 11-14, 16-18 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The specification provides adequate written description for SEQ ID NO:1 and SEQ ID NO:4, but not variants.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116).

With the exception of SEQ ID Nos 1 and 4, the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides and polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See Fiers v. Revel, 25 USPQ2d 1601 at 1606 (CAFC 1993) and Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481 at 1483. In Fiddes, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only isolated polynucleotides comprising the sequence set forth in SEQ ID NO:1 and the isolated polypeptides comprising the amino acid sequence set forth in SEQ ID NO:4, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Conclusion

No claims are allowed

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Regina M. DeBerry whose telephone number is (703) 305-6915. The examiner can normally be reached on Mondays-Fridays 8:00 a.m. - 4:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (703) 308-4623. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

RMD
December 10, 2002

Elizabeth C. Kemmerer

ELIZABETH KEMMERER
PRIMARY EXAMINER